

REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office action dated November 4, 2005 are respectfully requested.

I. Amendments

Claim 11 is amended to depend from claim 10.

Claim 45 is amended to recite specific conditions which are responsive to treatment by rapamycin. Basis for these amendments can be found on page 23, line 19 through page 24, line 10.

No new matter is added by way of these amendments.

II. Rejections under 35 U.S.C. §112, second paragraph

Claims 11 and 45 were rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 11 is amended in accord with the Examiner's kind suggestion.

Claim 45 is amended in accord with the Examiner's kind suggestion to list the conditions intended.

In light of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §112, second paragraph.

III. Rejections under 35 U.S.C. §103

Claims 1, 10-19 and 45 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Cottens *et al.* (U.S. Patent No. 5,912,253).

Applicants respectfully traverse these rejections.

A. The Present Invention

Claim 1, as amended, relates to a 42-O-ethoxyethyl rapamycin compound (claim 1). Claim 10 relates to a pharmaceutical composition comprising the 42-O-ethoxyethyl rapamycin compound.

B. The Cited Art

COTTENS ET AL. describe demethoxy derivatives of rapamycin.

C. Analysis

The present claims are directed to a 42-O-ethoxyethyl rapamycin and method of treatment comprising administering the compound. Cottens *et al.* fail to show or suggest such a compound or pharmaceutical composition comprising such a compound.

"Obvious-to-try" is not the standard of obviousness. Obvious to try would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In re O'Farrell 853 F2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988). In re Antoine, 559 F2d 621, 195 USPQ 6 (CCPA 1977). In re Goodwin, 576 F2d 375, 198 USPQ 1 (CCPA 1978). Cottens *et al.* describe demethoxy derivatives of rapamycin having the structure of Formula I (see Col. 2, line 30). From this formula, there are thousands of possibilities among the described chemical groups. Nothing in the teaching of Cottens *et al.* would lead one skilled in the art to the presently claimed compound. It should be noted that even rapamycin is encompassed by the parameters of the Cottens *et al.* formula. Cottens *et al.* also describe 15 "especially preferred" compounds (see Col. 5, lines 12-37), none of which would lead one to the presently claimed compound as they are all demethoxy derivatives.

The Office action states "the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties" (see page 3 of Office action mailed November 4, 2005). However, a skilled chemist would expect significant variance in the properties of the compounds disclosed in Cottens *et al.* and the presently claimed compound.

As evidenced by the teaching in Cottens *et al.*, derivatives of rapamycin that are similar in structure do not necessarily have similar properties. Cottens *et al.*

disclose that the "novel compounds" were "up to 3x more active than rapamycin" in the mixed lymphocyte reaction (see Col. 8, lines 60-61). The "novel compounds" were "up to 5x more active than rapamycin" in the IL-6 mediated proliferation test (see Col. 9, lines 15-16).

The presently claimed compound also shows significant and unexpected efficacy over either rapamycin or everolimus (a rapamycin derivative). As detailed in Example 5 of the present application, neointimal area and diameter stenosis were compared with in vivo stent placements for each of rapamycin, everolimus and 42-O-(ethoxyethyl) rapamycin. As seen in Table 1 on page 30, neointimal area for rapamycin at 2 doses was 2.8-3.75, ranged from 2.97-3.54 for everolimus at three doses, and was 1.30 mm² for the claimed compound. Additionally, the percent diameter stenosis was much lower for the claimed compound (14.8%) as compared to either rapamycin (43.0-55.0%) or everolimus (38.0-53.0%). In view of the unexpectedly higher efficacy of the claimed compound over the structurally related rapamycin and everolimus, it cannot be said that the present compound is obvious over a teaching of structurally related compounds.

In view of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

IV. Statutory Double Patenting Rejection under 35 U.S.C. § 101

Claims 1 was provisionally rejected under the 35 U.S.C. § 101 as claiming the same invention as claim 6 of co-pending Application No. 10/987,771. Applicants will address this rejection at such time as allowable claims are found in this or the co-owned application.

Conclusion

Applicants respectfully submit that the pending claims are in condition for immediate allowance. The undersigned invites the Examiner to call (650) 838-4410 with any questions or comments. The Commissioner is hereby authorized and

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Attorney Docket No. 38779-8002.US00

requested to charge any deficiency in fees herein to Deposit Account No. 50-2207 to facilitate entry and consideration of this Amendment.

Respectfully submitted,
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Date: February 6, 2006

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